

## **REMARKS**

### **I. Status of Claims**

Claims 1, 2, and 4-16 are currently pending, and stand rejected. Claims 1 and 2 have been amended. Claims 14-16 have been cancelled without prejudice or disclaimer. Claims 1 and 2 have been amended to delete the term “derivative”. Claims 1 and 2 have also been amended to define R as per the Examiner’s suggestion. Claims 1 and 2 have been further amended to recite “inorganic acid additive.” No new matter has been added.

### **II. Claim Objections**

Claim 16 has been objected to. Claim 16 has been cancelled without prejudice or disclaimer, rendering the objection moot. Withdrawal of this objection is respectfully requested.

### **III. Claim Rejections**

#### **a) Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1, 2, and 4-16 stand rejected as being indefinite. Without conceding the correctness of the Examiner’s position or the need for amendment, Applicants have amended claims 1 and 2 to delete the term “derivative”. Thus, claims 1 and 2, and claims 4-13 which depend either directly or indirectly from claim 1, no longer contain allegedly indefinite terms. Applicants respectfully request reconsideration and withdrawal of this rejection.

**b) Rejections Under 35 U.S.C. § 103(a)**

Claims 1-2 and 14-16 stand rejected as obvious in view of Kwak et al. (WO 02/10147, "Kwak") in view of Aslam et al. (Kirk – Othermer Eyclopedia of Chemical Technology, 12/4/2000, p. 477, "Aslam"). Applicants respectfully traverse.

The Examiner contends that Kwak allegedly discloses the continuous process for producing optically pure (S)-beta-hydroxy-gamma-butyrolactone. The Examiner further contends that the esterification reaction is carried out at 50 to 150° C in the presence of a catalyst such as a solid acid of a sulfonate-substituted strong acid resin. The Examiner concedes that the instant invention differs from the prior art in that the inorganic acid catalyst is unspecified in the esterification process, as it its amount.

The Examiner further contends that Aslam allegedly discloses the use of the various catalysts in the esterification process. The Examiner also states that Aslam discloses the amount of the inorganic acid used in the process, and the limitation of a process with respect to ranges of pH, time and concentration, when such values are those which are determined during routine optimization.

The Examiner concludes that Kwak allegedly discloses the continuous process for producing optically pure (S)-beta-hydroxy-gamma-butyrolactone by using the esterification step in the presence of a solid acid, and Aslam allegedly discloses that there is an equivalence between the sulfuric acid or hydrochloric acid and the solid acid catalyst in the esterification process.

The Examiner further concludes that it would have been obvious to incorporate the Aslam sulfuric acid catalyst into the Kwak process as an alternative to the solid acid catalyst. This is because, the Examiner states, one of ordinary skill would expect such a manipulation to be successful, based on the cited art. Applicants respectfully traverse.

The Applicants' arguments regarding the § 102(a) rejection in view of Kwak have resulted in a withdrawal of the § 102(a) rejection. Therefore it is concluded that the claim set filed with the amendment of November 28, 2007 is not anticipated by Kwak. Applicants respectfully request acknowledgement of this fact, as there is not a § 102(a) rejection in the instant Office Action.

With regard to the obviousness rejection of Kwak in view of Aslam, Applicants submit the following arguments.

The Examiner stated that Kwak allegedly discloses a continuous process for producing optically pure (S)-beta-hydroxy-gamma-butyrolactone, in which the esterification reaction is carried out at 50 to 150°C in the presence of a catalyst such as a solid acid or a sulfonate-substituted strong acid resin; whereas Aslam allegedly discloses the use of various catalysts in the esterification process, and concludes that it would have been obvious to one of ordinary skill in the art to be motivated to incorporate the sulfuric acid catalyst of Aslam, into the Kwak process as an alternative to Kwak's solid acid catalyst.

The present invention describes dissolving carboxylic acid ester of Formula 2 in solvent to which has been added an organic or inorganic acid additive specifically for the production of

chemically pure (S)-beta-hydroxy-gamma-butyrolactone having a specific desired optical activity. Neither Kwak nor Aslam, alone or in combination, disclose, suggest, or provide a motivation to use an organic or inorganic acid additive in solvent for dissolving carboxylic acid ester.

The present invention aims to increase the optical purity of an initial product in a continuous hydrogenation process by adding an organic or inorganic acid additive, such as formic acid, oxalic acid, malic acid, acetic acid, and so on, added to the solvent required for the hydrogenation.

According to the prior art literature regarding oxidative dehydrogenation, it is reported that oxidation (dehydrogenation) does not occur under strong acidic conditions (Coord. Chem. Rev. 1999, 187, 121).

However, the carboxylic acid ester used in the present invention contains a secondary alcohol moiety therein, and thus, during hydrogenation by metal catalyst, partial racemization occurs by oxidation (dehydrogenation) and reduction (hydrogenation) of the secondary alcohol moiety, thereby decreasing optical purity. So, with the aim of overcoming the problems related to racemization, an acid is introduced to the solvent as an additive.

In producing (S)-beta-hydroxy-gamma-butyrolactone having high optical purity (ee > 99.0%), the prior art literature does not report such employment of the acid for the hydrogenation of the carboxylic acid ester (*See* page 8, line 11 to page 9, line 7 in the PCT publication of the present application).

In this regard, Examples 3-6 and 15-22 in the Specification as file of the present application show that when using solvent containing an acid additive in accordance with the present invention (Examples 3-5), a desired optical purity at the initial reaction stage ( $ee > 99.0\%$ ) was obtained, but when the acid additive was not used (Examples 6 and 15-22), the optical purity was lowered.

The Examiner has overlooked this aspect of adding an acid additive to produce, via hydrogenation reaction, chemically pure (S)-beta-hydroxy-gamma-butyrolactone having increased optical activity, which has been obtained with the instant invention.

Kwak clearly fails to disclose, suggest, or provide a motivation to use an acid additive in the hydrogenation of substituted carboxylic acid, either alone or in combination with Aslam. The present invention discloses adding an acid additive in the solvent for hydrogenation in order to increase the optical purity at the initial reaction stage.

Applicants respectfully request reconsideration and withdrawal of this rejection.

**CONCLUSION**

In view of the foregoing amendments and remarks, Applicants believe the pending application is in condition for allowance, and earnestly solicit same.

If the Examiner feels that any remaining issues can be resolved through a Supplemental Amendment or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

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Respectfully submitted,

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